

May 13, 1957

Dear Luca:

I am of course waiting to hear from you about your plans for visiting the U.S. this summer, and also whether you can accept our invitation to the Medical Genetics Symposium. But meanwhile, I thought you might be vitally interested in the book for which I enclose the advertisement.

I have had a chance to look at it. At first I wondered if it might not be close enough to our own enterprise to interfere, but on further examination I don't think so. Actually there are only about 10 pages on genetic mechanisms and this is none too good. All the more reason to do a good job in that area! The authors are extremely uncritical. Mainly, they just summarize the quoted views of the other workers. Their own conclusion, as far as they have one is:

The great variability of bacteria and the high sensitivity of their...functions to environmental changes might influence the formation or nature of premutative cells and become the cause of different types of bacterial drug fastness....Induced mutation therefore is able to explain many of the phenomena of drug resistance as they appear at the present time. p.353

In fact, the more I read this, the more dangerous and insidious a work this seems. It has some color of authoritativeness, as it quotes a wide range of observations, but how they can draw such conclusions, except in an effort to reconcile contradictory hypotheses of the other workers.

On the other hand, the book does have a great deal of material on the auxiliary aspects of biochemical mechanisms of resistance, its incidence in many different organisms (including a great deal with protozoa), and it will warrant careful study to judge how far to re-approach the same issues. On the whole, I think we should not deviate very much from our original plans, except to regard this a) as a subtle counterfoil, and b) as a useful source for some of the material of secondary interest to us.

Here's another:

"Whether [replica-plating; indirect selection] proves unequivocally the presence of naturally occurring mutants of high resistance will not be discussed here."

"The most important point in the interpretation of the genetic mechanisms of drugs resistance is still the fact that in at least one stage of the observations exposure of the organisms to a toxic agent has to take place." p.216 Of course this is particularly false in the case of constitutive-penicillinase mutants of *B. cereus*, and is a specious argument at best. The whole sorry business does illustrate how careful we shall have to be in stating our problems.

Yours,

